USDA Agricultural Research Service
U.S. DEPARTMENT OF AGRICULTURE

Antimicrobial Resistance Research Strategy

Contents

Executive Summary

Increases in bacteria with antimicrobial resistance (AMR) are a threat to animal, plant, environmental, and public health. National and international strategies have been developed to address this issue. In 2015, the World Health Organization published the **Global Action Plan** on AMR. In 2019, the Centers for Disease Control and Prevention (CDC) released the **AMR Threats Report** (Antibiotic Resistance Threats in the United States) identifying AMR bacteria of urgent concern. In 2020, a new **National Action Plan** for combating antibiotic resistant bacteria (CARB) was released. All these actions highlight the need for prioritized research focused on identifying and reducing health risks of crucial importance associated with AMR in agriculture. These documents also highlight the need for research and collaboration across multiple sectors to 1) inform the science community of data to fill critical research gaps, 2) develop science-based strategies to reduce AMR of crucial importance associated with agriculture, and 3) communicate solutions.

As the intramural research arm of the U.S. Department of Agriculture (USDA), the Agricultural Research Service (ARS) conducts solution-oriented, hypothesis-driven research to solve agricultural problems of high national priority. ARS is the lead U.S. government agricultural agency conducting non-regulatory research to characterize, target, and mitigate AMR associated with agriculture. ARS develops alternatives to antimicrobials (ATA) that reduce the need for antibiotics in agricultural settings. In 2021, ARS hosted a "Research Solutions for AMR Workshop" to learn from key stakeholders and research partners about the state of the science and to identify industry and regulatory research priorities on AMR in agriculture. ARS scientific experts across the One Health spectrum — which includes animal, plant, environment, and food safety/public health — collaborated to identify ARS research needs and priorities, which resulted in the development of this 2023 ARS AMR Research Strategy.

USDA-ARS Antimicrobial Resistance Research Strategy

This AMR Strategy identifies priorities and objectives to detect, prevent, and control AMR and to develop ATA. It outlines four interrelated priorities for ARS:

Risk Detection

Develop risk tools and models to assess AMR drivers across agricultural settings and develop predictive analysis abilities to optimize processes for addressing AMR.

Systems Biology & Detection Strategies

Identify strategies to reduce AMR of crucial importance by developing rapid, innovative, and user-friendly technologies and data exchange and analytic tools to populate decision support and risk models, disease diagnostics, and rapid detection.

Mitigation

Develop novel intervention strategies, innovative user-friendly technologies, and ATA to optimize antibiotic use and/or reduce AMR transmission.

Science Outreach

Foster collaboration, community building, and communication around ARS AMR research to enhance solution-based AMR research that prioritizes risks, enhances understanding, and improves AMR detection and control.

Introduction

ARS AMR Vision

Be the global leader for innovative, equitable, sustainable research solutions for AMR in agriculture.

ARS AMR Mission

To promote the resilience of agriculture to AMR for the health and safety of animals, plants, environment and the U.S. public through cutting-edge research solutions and outreach

Antimicrobial resistance (AMR) poses a serious threat to plant, animal, and environmental health; food safety; and public health, all of which are collectively known as "One Health." AMR is complicated because many genes encoding AMR are ancient and widespread across many different bacterial species, and factors other than antibiotic use can support the increase of AMR bacterial populations. Bacterial pathogens with AMR can increase health risks within the One Health spectrum because resistance interferes with the efficacy of traditional therapeutic treatments. Consequently, there is a critical need to develop innovative strategies and tools that mitigate AMR of critical importance to animal, plant, environmental, and public health, and to develop alternatives to antimicrobials (ATA) that reduce the need for antibiotics in agriculture.

The Agricultural Research Service (ARS) is the in-house non-regulatory research agency of the U.S. Department of Agriculture (USDA) and is the only agency within the Federal government charged with researching, developing, and transferring solutions to agricultural problems of high national priority. ARS is uniquely positioned with a diverse multidisciplinary workforce that can conduct multifaceted and long-term longitudinal studies across complex agricultural systems. As a result, ARS has generated a strong track record of solution-oriented, hypothesis-driven research delivering innovative, equitable, and sustainable AMR solutions.

In 2012, the **USDA Antimicrobial Resistance Action Plan** was developed based on input from stakeholders. Subsequently, given the changing landscape of AMR research, ARS hosted a "Research Solutions for AMR Workshop" in 2021, which included participants from all ARS four national program areas (Animal Production and Protection; Crop Production and Protection; Natural Resources and Sustainable Agriculture Systems; and Nutrition, Food Safety and Quality). Workshop participants were charged with defining and prioritizing AMR and ATA research for the next 5 to 10 years, and stakeholders and partners were invited to speak about the state of the science in AMR. As a result, ARS scientists developed the AMR vision and mission statements and identified research priorities to ensure ARS AMR/ATA research remains cutting edge, solution oriented and priority focused.

Priority 1: Risk Detection

Goal: Develop risk tools and models to assess AMR drivers across agricultural settings and develop predictive analysis abilities to optimize processes for addressing AMR.

Background

Prioritizing the most critical AMR risks associated with agriculture and devising targeted interventions requires research and science-based data for hazard identification, exposure assessment, and risk characterization. The lack of science-based risk analysis limits the predictive capabilities of risk models that both inform risk assessments and identify control points for targeted intervention. Interventions must be based on reliable model outputs to effectively reduce the emergence and spread of the most significant AMR risks associated with agriculture. Integrated approaches are needed, incorporating data across agricultural landscapes, commodities and management practices.

The complexity of agricultural landscapes must be considered to obtain science-based information for robust models that aid in hazard identification and to inform risk analyses and generate quantitative or qualitative risk scores identifying factors that select for the most significant AMR. These approaches will enable the ranking of AMR risks, identify factors that promote AMR, and will help prioritize the development of interventions. There is a need to identify AMR hazards (potential to be harmful) through risk analysis (i.e., identifying risk and assigning it a quantitative or qualitative risk score) and assess the risks' potential impact for purposes of prioritization of intervention. Reliable risk analyses are needed to inform these robust national and global risk assessments and to facilitate addressing the highest priority risks associated with AMR.

To effectively address AMR hazards, risks, and dynamics, each needs to be properly identified, assessed, and prioritized through the One Health approach. Defining AMR risks and hazards as they relate to animals, plants, the environment, and food safety is the first step in this process.

Objectives

1.1 Define and identify AMR risks and hazards in agricultural and public health sectors

- Quantify and model agricultural AMR hazards to identify AMR pathogen risks that correlate most closely with negative health outcomes and identify control points for interventions.
- Apply data obtained with innovative technologies incorporating systems biology and artificial intelligence approaches to define the terminology and importance of AMR hazards and AMR risks.
- Design models and predictive tools for the early detection and identification of new and emerging AMR risks that threaten all sectors.
- Conduct research to assess AMR risk levels by identifying and defining hazards to prioritize the critically important risks.

1.2 Develop AMR risk models to assess AMR drivers across agricultural and public health sectors

- Develop standardized tools to improve data collection and management to inform AMR risk models.
- Develop risk models that can harmonize with national and international guidelines.
- Work across disciplines to develop approaches to identify data and information technology tools used for predictive analytics and system biology approaches.
- Collect and input data from systems biology studies into risk models to improve predictive ability and identification of AMR reservoirs that are factors driving the development of resistance.
- Utilize alternatives to traditional risk assessment models, such as structured decision making, to develop more qualitative, rather than quantitative, risk assessments.

1.3 Link AMR risk data to the impact of interventions

- Design multidisciplinary studies and use data to inform risk models and enhance predictive tools to identify high impact, high reward interventions.
- Utilize artificial intelligence to predict outcomes from mitigation strategies and to predict emerging AMR risks and hazards.
- Prioritize research outcomes to provide equitable solutions across agricultural and public health sectors.
- Integrate research outcomes and predictive data and evaluate risks to inform decisions.

Anticipated Outcomes

- Enhanced ability to recommend interventions that reduce the prevalence of the highest risk AMR pathogens and predict emergence of new resistance mechanisms in production agricultural systems.
- Identification of AMR bacteria that present critical risk while their prevalence is still low enough to respond to interventions.
- Risk assessment approaches and assessments that provide an understanding of the impacts of AMR bacteria on food production and processing, as well as appropriate responses triggered by a fact-based decision matrix.
- Informed risk-assessment models that result in a comprehensive understanding of how AMR of critical importance to agriculture affects production and management.

Priority 2: Systems Biology & Detection Strategies

Goal: Identify strategies to reduce AMR of crucial importance by developing rapid, innovative, and user-friendly technologies, data exchanges, and analytic tools to populate decision support and risk models, disease diagnostics, and rapid detection.

Background

Agricultural systems are increasingly challenged by the need for food production and processing strategies for limiting the emergence and proliferation of AMR that threatens health and safety. Currently, there are inadequate rapid diagnostics and early detection methods for identifying bacterial strains and genes associated with AMR that are a risk to animal, plant, environmental, and public health. New technologies and approaches are needed to detect emerging AMR pathogens and dangerous new strains. Mitigation strategies targeting AMR require accurate and timely identification and assessment of AMR-linked genes and pathogens that cause disease.

Developing rapid, robust, user-friendly, and cost-effective technologies that provide real-time data needed for decision making will help inform interventions and prevent the emergence and spread of AMR pathogens associated with agriculture. Tools that provide early detection and meaningful measurements to inform risk models and lead to rapid recommendations regarding appropriate mitigation steps across agricultural systems will have the greatest impact.

By integrating data across agricultural systems and prioritizing effective data analytics, ARS can proactively help producers make sound, science-based management decisions that minimize proliferation of AMR threats of crucial importance to agricultural and public health sectors. Flexibility and harmonization must be prioritized to meet current and future stakeholder needs for food production systems that support animal, plant, environmental, and public health.

Objectives

2.1 Define technologies for rapid AMR detection in agricultural and public health sectors

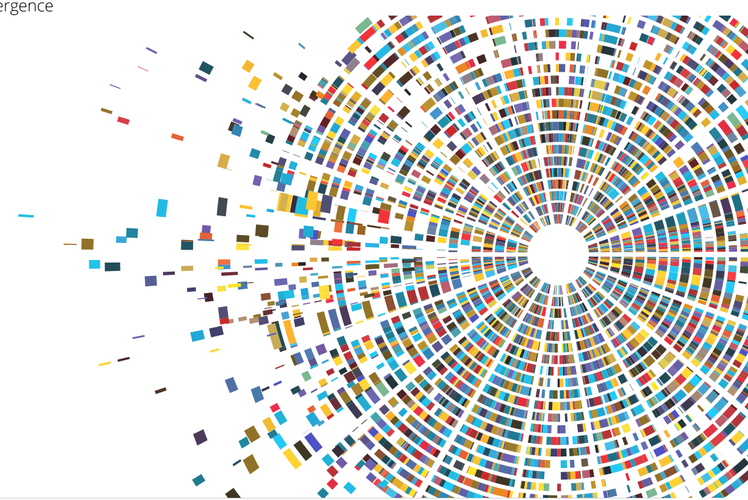
- Identify, develop, and evaluate assays for use in on-site disease diagnostics and detection and for monitoring AMR in pathogens of importance.
- Determine detection limits of rapid detection technologies.
- Provide end users with real-time information about the presence of prioritized AMR targets that could lead to the rise of AMR populations.
- Create low-cost, rapid, and accurate tools that can analyze a wide variety of sample types while yielding a rapid genotypic and/or phenotypic characterization of a sample.
- Develop tools to help identify trends by predicting the emergence and location of critically important AMR targets.

2.2 Facilitate the exchange of data and outcomes

- Develop standardized methodologies with data output can be easily shared.
- Compile information gathered by precision monitoring systems into a database for analysis with bioinformatics, computational biology, and artificial intelligence.
- Place current and historical data into an open-access database to facilitate hypothesis-driven research.

2.3 Advance strategies for using risk models and decision support systems to reduce and prevent critically important AMR, and develop strategies that predict the emergence of AMR and bacterial pathogen combinations with the greatest potential impact on agricultural and public health sectors

- Use sequence data and artificial intelligence analysis tools that enable the facile assessment of reservoirs and drivers of AMR of critical importance to inform interventions.
- Develop models that define the probability of AMR occurring and inform risk.
- Create informed decision matrices enabling stakeholders to make management choices that yield the best possible outcomes.

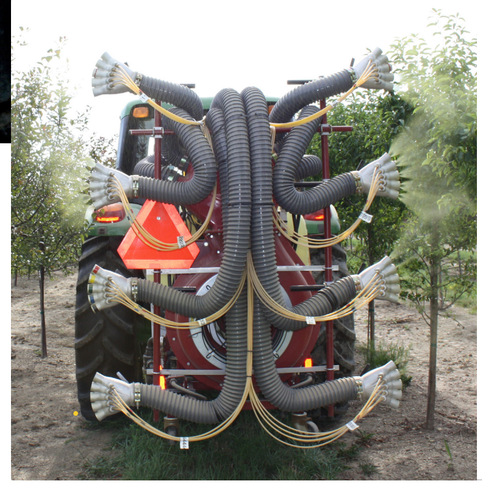


Anticipated Outcomes

- Development of field-deployable rapid diagnostic systems that report results, provide interpretations, and present putative action plans to the end user.
- Data from diagnostic systems are assembled into a standardized format that facilitates digitization of datasets.
- Improved sharing/accessibility of the databases, tools, and risk assessments created in response to the listed objectives.
- Creation of model systems that can identify critical AMR threats before they become established in U.S. agricultural production systems.

Priority 3: Mitigation

Goal: Develop novel intervention strategies, innovative, user-friendly technologies and ATA to reduce the need for antibiotic use or reduce AMR transmission.



Background

Successful and sustainable agriculture depends on healthy, resilient systems. To mitigate increases in AMR bacteria, many agricultural production systems judiciously use antibiotics, antibiotic rotation or antibiotic combinations, or integrate antibiotics use with non-antibiotic therapies. However, these practices introduce varying degrees of risk for potentially transmitting AMR genes and bacteria within the One Health spectrum.

Research investigating the genetics of health — such as selecting for or designing organisms with genetic resistance to disease — will help with reducing AMR, as will research identifying elements of production system environments and microbiomes that keep pathogens at bay and promote health. Information is needed about the national and international complexities of agricultural production systems so that effective precision management approaches minimizing AMR and maintaining healthy production systems can be developed. Artificial intelligence has generated the prediction of an array of new antibiotics and antimicrobial compounds already existing in nature; research is needed to find these compounds and assess their potential use in maintaining healthy agricultural systems.

Finally, research is needed on identifying new ways to block the transmission of AMR bacteria or AMR genes throughout the One Health continuum; this information could support interventions that actively reduce the frequency of AMR bacteria and genes in production environments. All these research avenues have the potential to significantly mitigate AMR, harness the depth and talent within ARS to serve stakeholders, and promote healthy agricultural systems.

Objectives

3.1 Reduce pathogens and diseases that lead to critically important AMR in agricultural and public health sectors

- Identify host disease resistance determinants.
- Define characteristics of healthy hosts, healthy immune responses, microbiomes, and the resistome.
- Manipulate microbiomes with genetic engineering and competitive exclusion.
- Improve breeding and genomics to obtain disease resistance.
- Perform regional, national, and global surveys to identify best practices across agricultural production and processing systems to maintain animal, plant, environmental, and public health.

3.2 Develop precision management techniques that optimize health and minimize AMR impacts of crucial importance across agricultural and public health sectors

- Develop integrated models to optimize scheduling for prophylactic applications and interventions for specific diseases.
- Use precision agriculture technologies to optimize antibiotic applications.
- Develop multidisciplinary food processing approaches to reduce human pathogens in processed foods.
- Genetically engineer microbes and phages with enhanced disease control capabilities to target AMR organisms of interest.

3.3 Develop new ATA, drugs and tools to control disease without increasing AMR

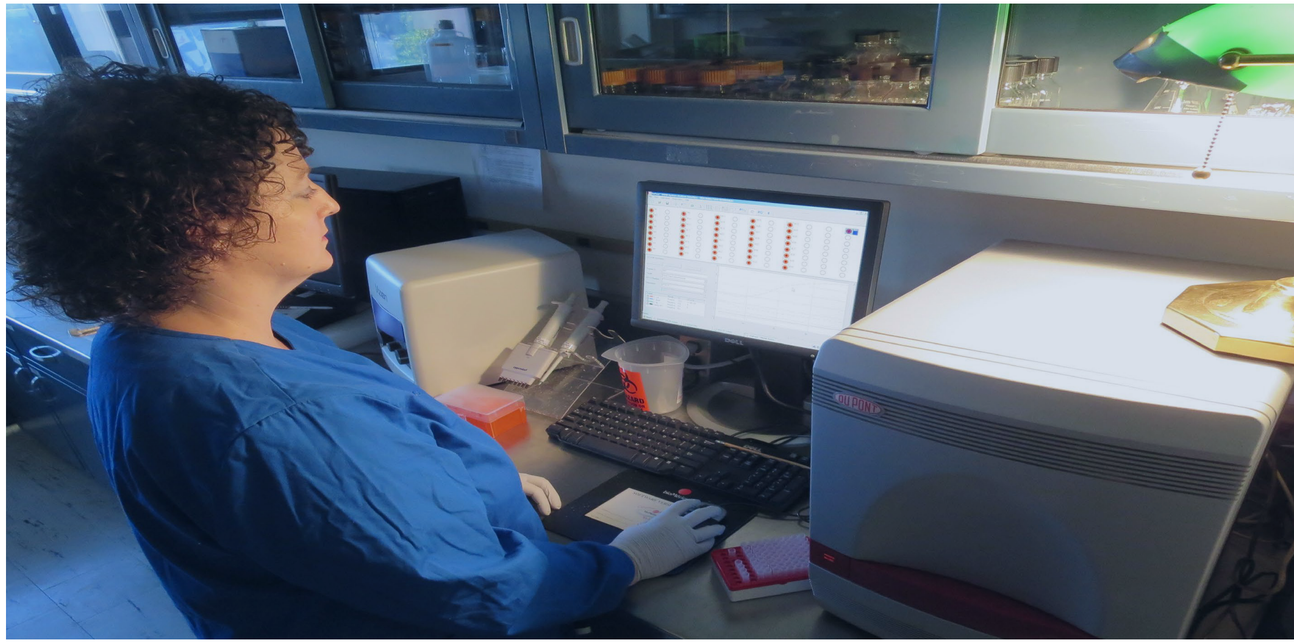
- Develop preventive and treatment strategies against major diseases that predispose antibiotic use.
- Design and screen compounds using artificial intelligence and machine learning to discover new drugs, antibiotics, and antimicrobials.
- Develop new food processing sanitizers and technologies to reduce transmission of food borne pathogens.

3.4 Develop optimized intervention strategies that reduce the levels, occurrence, and transmission of AMR in pathogens of importance in agricultural and public health sectors

- Improve food processing interventions.
- Develop strategies that reduce pathogen loads entering the environment or the food system.
- Evaluate the effect of integrated and/or multi-hurdle interventions on AMR levels and persistence.

Anticipated Outcomes

- AMR mitigation solutions will be economically feasible, widely available, and scalable, from micro-farms to large production systems.
- Reduction of microbial diseases and foodborne pathogens in agricultural ecosystems.
- Discovery and/or development of antibiotics and ATA for long-term, efficacious disease management.
- Development of management strategies to reduce critically important AMR transmission.
- The use of artificial intelligence to maintain optimal animal, plant, environmental, and public health and to create and design new therapeutics.



Priority 4: Science Outreach

Goal: Foster collaboration, community building, and communication around ARS AMR research to enhance solution-based research to prioritize risk, enhance understanding, improve detection, and control AMR.

Background

Combating AMR requires communicating science-based information and solutions to diverse stakeholder groups quickly and effectively, which will help address issues created by a critical lack of data, resources, and capacity building. AMR research must be complemented by coordinated action with stakeholders to ensure that emerging AMR strains are rapidly detected, diagnosed, and contained at the source. Improving capacity for quick and user-focused data communication is necessary for promoting innovative mitigation strategies such as drug and vaccine development; it will also strengthen AMR detection and diagnostic systems and ensure field reporting is timely, accurate, and transparent. Improving early and routine communication with commodity groups and the public regarding new or emerging AMR concerns and their potential impact is an essential component of AMR research and mitigation.

Objectives

4.1 Use communication platforms to build public awareness about AMR research in ARS

- Develop strategies to inform stakeholders about ARS information on critical AMR risks and challenges, best practices, and opportunities.
- Engage with science and community communication and social science experts to enable efficient, effective, and topical AMR communications to agricultural and public health sectors.
- Assemble, synthesize, interpret, and communicate relevant information effectively and in user-friendly formats.
- Integrate AMR science into messaging tools such as research publications, gray literature, pamphlets, dashboards, social and other media communications, and video and podcast products and ensure all messaging meets **Section 508 Accessibility and Compliance | USDA requirements**.

4.2 Promote disseminating information needed to effectively address AMR

- Improve data standardization and increase data availability.
- Broaden the scope of AMR stakeholders and partners receiving AMR communications.
- Establish collaborations and partnerships to incentivize development of rapid detection tools and new therapeutics to mitigate AMR.
- Develop educational modules, webinars, workshops, trainings, and demonstration projects that follow Section **508 Accessibility and Compliance | USDA regulations**.
- Participate in and lead regional and national working groups and initiatives on AMR information syntheses and interpretation.

4.3 Develop a central location for AMR communication

- Establish a location to provide information on ARS AMR activities.
- Execute risk-informed, accurate, timely, and actionable public messaging.
- Promote clear, consistent, and coordinated messaging to inform AMR stakeholders and partners.

Anticipated Outcomes

- Story maps, dashboards, and other virtual and web-based communication tools to promote innovative and creative AMR research.
- Virtual ARS AMR communication networks that disseminate equitable information to AMR stakeholders and partners.
- A comprehensive ARS AMR/ATA database minimizing research redundancies and enabling ARS scientists to conduct meta-analyses of available data.
- Tools identifying ARS scientists who have expertise that could support ARS AMR research but who do not include AMR research in their project plan.
- Improved communication among ARS scientists across disciplines, improved interagency communications, and broader communication with diverse stakeholder groups.

Challenges

The challenges to controlling AMR and implementing AMR research across the One Health Spectrum are well documented in many studies and documents including the **CARB 2020-2025 National Action Plan** and **National Academies Reports**. Detailed below are specific challenges that ARS faces in implementing AMR research.

Agriculture is diverse and very complex with a myriad of stakeholders, including farmers, producers and ultimately the American consumer. Research solutions must be economical and practical to facilitate adoption so as not to contribute to rising food costs and food insecurity. Additionally, given the complexity of plant, animal and other agricultural systems, what may work in one system, may not work in another, thus solutions must be tailored to address each production system individually. This requires the collaboration of scientists with expertise in multiple disciplines, cooperation, trust, and engagement from multiple stakeholders and if required, navigation of multiple regulatory pathways. In comparison to public health, agriculture has received fewer resources to combat antimicrobial resistance.

Conclusions

USDA-ARS possesses in-depth knowledge about management practices and technologies associated with animal, plant, environmental, and public health and is uniquely positioned to contribute to the body of scientific knowledge around AMR. The goal of eliminating AMR completely is unrealistic, but AMR can and must be managed. Mitigating AMR requires a science-based comprehensive approach to minimizing risks of crucial importance and creating real-time detection technologies. ARS will use this AMR Strategy to optimize its own efforts and harness the work of essential stakeholders and partners to understand, detect, and mitigate AMR that can harm agricultural and public health. This strategy outlines a comprehensive and integrated approach for future ARS AMR priorities that were developed during its' 2021 "Research Solutions for AMR Workshop." The successful execution of this strategy will provide and disseminate innovative, equitable, and sustainable AMR solutions that will protect consumers, support stakeholders, and improve agricultural production systems.

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